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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/103,745	06/24/1998	SUDHIR AGRAWAL	475.08.642CI	3401
7590 01/25/2006 WAYNE A KEOWN HALE AND DORR 60 STATE STREET BOSTON, MA 02109			EXAMINER SCHULTZ, JAMES	
			ART UNIT 1635	PAPER NUMBER
DATE MAILED: 01/25/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/103,745

Applicant(s)

AGRAWAL, SUDHIR

Examiner

J. D. Schultz, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 October 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 3-5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

Applicant's response filed 28 October 2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 24 August 2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Response to Arguments, Double Patenting***

Claims 1, and 3-5 are the rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,856,462 for the same reasons of record cited in the Office action mailed September 9, 1999. While the rejection is maintained, it is acknowledged that Applicant's response to the instant rejection indicated that, should any pending claims be indicated as allowable, applicant will file a Terminal Disclaimer disclaiming the portion of the term of the patent beyond the expiration date of U.S. Patent Number 5,856,462.

### ***Response to Arguments--Claim Rejections - 35 USC § 102***

Claims 1 and 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Cook (U. S. Patent Number 5,212,295) and is repeated for the same reasons as cited in the action mailed 1 July 2004.

The invention of the above claims is drawn to a composition comprising a phosphorothioate oligonucleotide that further comprises a modified CpG motif, wherein said modification is selected from the group consisting of alkylphosphonate, 2'-O, stereospecific phosphorothioate, phosphotriester, phosphoramidate, and 2'-5' CpG motifs. The invention is also drawn to methods of reducing the side effects of the administration of antisense oligos comprising administering antisense oligos which comprise the aforementioned CpG modifications.

As stated in the previous action, Cook teaches compositions comprising phosphorothioate oligonucleotides that further comprise modified CpG motifs, wherein said modifications are selected from the group consisting of alkylphosphonate, 2'-O, stereospecific phosphorothioate, phosphotriester, and phosphoramidate CpG motifs. Although Cook contemplates the use of such compositions in methods of treating disease, Cook does not explicitly teach that such methods would reduce the side effects of the administration of antisense oligos. However, because both the instant method steps and those of Cook comprise the sole active step of administering the subject oligos, the method of Cook would thus be considered to have the inherent outcome of reducing side effects accordingly, Cook is thus considered to anticipate both the instant compound claims as well as the method claims.

Applicants traverse this rejection by asserting that Cook fails to teach the claimed compounds and methods, because Cook fails to specifically teach CpG-containing phosphorothioate oligonucleotides, in general, as well as the claimed specific modifications to such oligonucleotides, in particular. This is considered to be factually incorrect, because the invention of the patent is focused on teaching how to make chirally pure phosphorothioate

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oligonucleotides, which are considered to be stereospecific phosphorothioate oligonucleotides.

Furthermore, at least one of the sequences disclosed therein contains the claimed CpG motif.

The basic formula for a CpG motif has been described (Mutwiri et al., pg. 90, enclosed) as comprising a 5'-X<sub>1</sub>X<sub>2</sub>CGY<sub>1</sub>Y<sub>2</sub>-3' motif, where X<sub>1</sub> is a purine, X<sub>2</sub> is a purine or a T, while Y<sub>1</sub> and Y<sub>2</sub> are pyrimidines. In this context, the disclosure of the exemplary oligo of column 13, lines 12-13, which comprises an ATCGCT motif that meets the above definition, is considered to teach at least stereospecific phosphorothioate CpG containing modified oligonucleotides, precisely as claimed. Because this oligonucleotide is disclosed as an antisense therapeutic, which must necessarily be administered to an animal as claimed, Cook et al. is considered to teach methods of administering an all ago of the instantly claimed invention which is presumed to be capable of in achieving the intended use as claimed.

Applicants indicate that the Cook patent's reference to "CPG" is with regard to controlled pore glass (CPG) supports which are standard solid state supports for oligonucleotide synthesis. While it is true that this comprises one reference to a CPG, it is not the only reference, since Cook otherwise teaches at least one oligonucleotide comprising a CpG motif as discussed above. The fact that Cook et al. does not disclose such an oligonucleotide as reducing side effects is not considered to alter its anticipatory teaching, since said oligo has all the structural limitations claimed, it is presumed to have the function of reducing side effects.

Applicant's contention that the oligonucleotide sequences provided by Cook, at col. 13, lines 6-15, are neither taught to be phosphorothioate oligonucleotides, nor taught to contain the claimed modifications at one or more of their CpG dinucleoside linkages seems to be contradicted by their very next argument, which states that the teachings of Cook generally

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instruct the production of chirally pure phosphorothioate or methylphosphonate or phosphotriester or phosphoramidate oligonucleotides. In fact, Cook indeed discloses that the oligonucleotides of his invention are chirally pure phosphorothioate or methylphosphonate or phosphotriester or phosphoramidate oligonucleotides, and indicates the oligonucleotides of column 13 are examples that may be so modified.

Finally, applicants allege that Cook does not teach the claimed specific combination of racemic phosphorothioate-containing-CpG linkage modified oligonucleotides of the invention. However, no racemic mixture is claimed. Applicants thus appear to be arguing limitations that are not found in the claims. Regardless, the claims recite that, among other limitations, the oligonucleotides of the instant invention may be stereospecific, which by the interpretation explained above would appear to stand in direct opposition to applicant's current contention that the claimed oligos are racemic in nature. The rejection is maintained accordingly.

### ***Conclusion***

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.


Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JDS

  
**J.D. SCHULTZ, PhD.**  
**PATENT EXAMINER**